UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/927,315	08/10/2001	Charles S. Zuker	02307E-120110US	4699

20350 7590 06/03/2004

TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
BRANNOCK, MICHAEL T	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 06/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/927,315	ZUKER ET AL.	
	Examiner	Art Unit	
	Michael Brannock	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *49-51 and 55-78* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *49-51 and 55-78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application: Claims and Amendments

Applicant is notified that the amendments put forth on 3/1/04, have been entered in full.

Response to Amendment

Applicant is notified that any outstanding objection or rejection that is not expressly maintained in this Office action has been withdrawn in view of Applicant's amendments.

Maintained Rejections:

Claims 49-51, 55-78 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the following reasons.

(A)The claims require "modulators" of taste transduction, however the specification does not set forth what a modulator is. At page 13 the specification sets forth that compounds can be activators, inhibitors, or modulators of taste transduction, thus it appears that the specification contemplates compounds that have properties other than that of an activator or inhibitor; what these properties are is not stated. Thus, the artisan would not know whether he or she was practicing the claimed invention.

Applicant argues that a definition of "modulator" is given in the specification. This argument has been fully considered but not deemed persuasive. The examiner can find no definition of "modulator" in the specification. Applicant argues that at page 10 it is stated that modulators may include activators, inhibitors, etc. This argument has been fully considered but not deemed persuasive. The specification is, at best, confusing in this regard because at page 14

line one it refers to activators, inhibitors, and modulators in the alternative; it gives definitions of activators and inhibitors, yet a definition of modulator is conspicuously absent.

(B) Claims 55-78 require a "functional effect", although the specification recites several examples of "functional effects" the skilled artisan could not be sure whether or not he or she was practicing the claimed invention because of the presence of such an ambiguous term.

Applicant argues that the examples provided in the specification provide sufficient detail to allow the metes and bounds of the claims to be determined. This argument has been fully considered but not deemed persuasive. Examples can not define the bounds of a concept; and the claims are not limited to those examples, thus the bounds of the claims are subject to the interpretation of the individual and are thus indefinite.

Claims 49-51, 55-78 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of identifying activators and inhibitors of sweet taste signal transduction, comprising a taste cell receptor composed of a heterodimer of SEQ ID NO: 9 and 15, wherein the receptor is present on the surface of a cell, and wherein the receptor is coupled to a Gα15 protein, does not reasonably provide enablement for methods employing artificially constructed variants of SEQ ID NO: 9 and 15, and nor for methods wherein the receptor is attached to a solid support, and nor for methods of identifying *modulators* of taste signal transduction. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

(A) The claims encompass the use polypeptide variants of the polypeptides of SEQ ID NO: 9 and 15 (substitutions, deletions or insertions in a protein corresponding to SEQ ID NO: 9 or 15) i.e. protein variants encoded polynucleotides that need only hybridize to a polynucleotide encoding SEQ ID NO: 9 and 15. Although the specification indicates that such variants are encompassed by the invention (e.g. page 5), no specific teaching is provided to indicate which amino acid substitutions, deletions or insertions to make. The specification has not provided sufficient guidance as to how to make and use the encoded polypeptides which are not 100% identical to the polypeptide of SEQ ID NO: 9 or 15, but which still retain a desired property of the polypeptide of SEQ ID NO: 9 or 15. Furthermore, the specification has not provided guidance as to what properties of the allelic variants or sequence variants of the protein corresponding to SEQ ID NO: 9 or 15 might be desired nor any guidance as to which amino acid substitutions, deletions or insertions to make to achieve any desired property. Applicant has not defined a difference in structure or difference in function between the proteins corresponding to SEQ ID NO: 9 and 15 and variants of said proteins. If a variant of a protein corresponding to SEQ ID NO: 9 or 15 is to have a structure and function similar to a protein corresponding to SEQ ID NO: 9 or 15, then the specification has failed to teach one of skill in the art which amino acid substitutions, deletions or insertions to make that will preserve the structure and function of a protein corresponding to SEQ ID NO: 9 or 15. Conversely, if a protein variant of SEQ ID NO: 9 or 15 need not have a disclosed property, the specification has failed to teach how to use such a variant.

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely

complex. While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These regions can tolerate only relatively conservative substitutions or no substitutions (see Bowie et al., 1990, Science 247:1306-1310, especially p.1306, column 2, paragraph 2). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions.

Although the specification provides the suggestion that such variants can be obtained, this is not adequate guidance as to the nature of active variants that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity.

The claims are, in essence, single means claims, because the claims encompass any composition having the recited activities whereas the instant specification only discloses those

naturally occurring compositions known to the inventor, i.e. SEQ ID NO: 9 and 15. In *In re Hyatt*, 708 F.2d 712, 218 USPQ 195 (Fed. Cir. 1983), a single means claim which covered every conceivable means for achieving the stated purpose was held nonenabling for the scope of the claim because the specification at most disclosed only those means known to the inventors. When claims depend on a recited property, a fact situation comparable to *Hyatt* is possible, where the claim covers every conceivable structure (means) for achieving the stated property (result) while the specification discloses at most only those known to the inventor. See also *Fiers v. Sugano*, 984 F.2d 164, 25 USPQ2d 1601 (Fed. Cir. 1993), and MPEP § 2164.08(a). With regard to enablement for artificially constructed variants of the polypeptides of SEQ ID NO: 9 and 15, the instant fact pattern is actually one step removed and deficient from that of *Hyatt*. The instant specification does not disclose any working examples of artificially constructed variants of the polypeptides encoded by SEQ ID NO: 9 and 15.

Applicant argues that the claims have been amended to require a functional effect, e.g. that the variant specifically binds a sweet receptor. This argument has been fully considered but not deemed persuasive. One of skill in the art understands that simply writing down or verbalizing that a protein should have a certain function in no way enables the artisan to obtain such a protein. The locations in the specification, pointed to by Applicant, simply recite generalize methodology that the artisan might use to try to find such sequences, however the skilled artisan understands that it is specific and not generalized information that is required, e.g. which positions can be substituted/added/deleted and which types of substitutions can be made at those positions. This information is completely lacking in the instant specification.

Applicants arguments regarding the weight to be placed on the lacking of working examples have been fully considered but are not persuasive. First, the lack of working examples of a variant is only one of many reasons provided in the rejection. Second, much weight should be placed on the fact that no working examples of a variant have been demonstrated or taught, because the use of such variants would make-up perhaps the largest portion of the claimed genus, and the artificially made variants are fundamentally different than the subgenera of naturally occurring proteins of which SEQ ID NO: 9 and 15 are but a single example.

(B) The claims encompass methods of identifying sweet taste modulators wherein the receptor is not present in the membrane of the cell, e.g. claim 62 requires that the receptor be attached to a solid support. Thus, the receptor would somehow need to make an appropriate response to a ligand when the receptor was attached to a solid support. No specific guidance is provided as to what methods can be used to accomplish this. The art recognizes the difficulty in establishing functional responses of taste receptor G-protein coupled receptors. It does not appear to be routine in the art to produce functional responses from such receptors in anything other than the membrane of the cell, see page 382, col 1, middle paragraph of Lindemann, B. Nature Medicine 5(4)381-382, for example. In this regard the claims are also single means claims, because the claims encompass any method having the recited activities whereas the instant specification only discloses the single method known to the inventor.

Applicant argues sweet taste signal transduction can be detected in various cell-free formats. This argument has been fully considered but not deemed persuasive, for the reasons discussed above. Further, arguments of counsel alone cannot take the place of evidence in the record once an examiner has advanced a reasonable basis for questioning the disclosure. See In

re Budnick, 537 F.2d at 538, 190 USPQ at 424; In re Schulze, 346 F.2d 600, 145 USPQ 716 (CCPA 1965); In re Cole, 326 F.2d 769, 140 USPQ 230 (CCPA 1964). Furthermore, "Tossing out the mere germ of an idea does not constitute enabling disclosure... [R]easonable detail must be provided in order to enable members of the public to understand and carry out the invention." Genentech, Inc. v. Novo Nordisk Inc., 108 F.3d 1361, 1366, 42 U.S.P.Q.2d 1001, 1005 (Fed. Cir. 1997).

(C) The specification puts forth that the sweet receptor can be coupled to a G-protein or a promiscuous Gα15 G-protein (see page12, line 23), however the only particular G-protein that is taught to work in the claimed invention is Gα15. The claims encompass, and the specification contemplates, using other G-proteins. The claims encompass the use of the endogenous G-protein(s) and the skilled artisan appreciates that such a use would be desirable, yet the specification has not provided any, and nor is such known in the prior art. Essentially, therefore, the specification has merely invited the skilled artisan to embark on an extensive research plan to try to find other G-proteins that would work in the invention. Such a call for extensive trial and error experimentation places an undue burden on the skilled artisan trying to practice the invention commensurate with the scope of what is being claimed. Additionally, in this regard the claims are also single means claims, because the claims encompass any method having the recited activities whereas the instant specification only discloses the single method known to the inventor.

Applicant argues that a G-protein is but one of potentially unlimited number of components that may be further used in addition to the sweet receptor. This argument has been

fully considered but not deemed persuasive. The use of a G-protein encompasses a substantial subgenus of Applicant's claims, yet is not adequately supported.

(D) As set forth above in item (A) of the rejection under 35 U.S.C. 112, second paragraph, the specification appears to make a distinction between the genus of compounds considered to be activators and inhibitors of sweet taste signal transduction and the genus of compounds that would be considered "modulators" of sweet taste transduction. It is unclear what this distinction is, if any. A reasonable interpretation is that "modulators" include the ability to transform the perception of taste from one quality to another, e.g. to "customize taste" (page 10, L25). For example, a modulator might, when present, make the taste of saccharin more like the taste of sucrose. Without trying to read limitations into the claims that are not there, one can only guess at what is intended to be encompassed by the intended distinction between "modulators" and "activated or inhibitors". Regardless, the specification has provided sufficient guidance only for assays that identify activators and inhibitors of sweet taste signal transduction as defined in the specification at page 13, L26 – page 14, L1.

Applicant's arguments regarding modulation have been fully considered but not persuasive. Applicant has not provided any detail as to how to determine if the signal transduction pathway could be affected anyway other than inhibition or activation.

Due to the large quantity of experimentation necessary to generate the infinite number of variants recited in the claims and screen same for activity, the lack of direction/guidance presented in the specification regarding G-proteins, solid supports and assays wherein the protein is not in a membrane, and modulators, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability

of the effects of mutation on protein structure and function and also the functionality of taste receptors in assay systems, and the breadth of the claims which fail to recite significant structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Conclusion

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (571) 272-0869. The examiner can normally be reached on Mondays through Fridays from 10:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, Ph.D., can be reached at (571) 272-0887.

Official papers filed by fax should be directed to (703) 872-9306. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB

June 1, 2004

LORRAINE SPECTOR
PRIMARY EXAMINER